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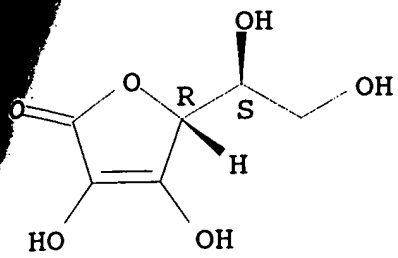


IC ICM A61K031-725
ICS C08B037-10
NCL 514056000
CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 1
IT **50-81-7, Ascorbic acid**, reactions
67-68-5, Dmso, reactions 546-67-8, Lead tetraacetate 7790-28-5, Sodium periodate
(oxidizing agent; heparin fractions for inhibiting thrombogenesis)

L55 ANSWER 6 OF 22 HCA COPYRIGHT 1998 ACS
124:259419 Usefulness of antioxidant vitamins in suspected acute myocardial infarction (the Indian experiment of infarct survival-3). Singh, Ram B.; Niaz, Mohammad A.; Rastogi, Shanti S.; Rastogi, Sharad (Centre Nutrition and Heart Research Laboratory, Medical Hospital and Research Centre, Moradabad, 244001, India). Am. J. Cardiol., 77(4), 232-6 (English) 1996. CODEN: AJCDAG. ISSN: 0002-9149.
AB In a randomized, double-blind, placebo-controlled trial, the effects of combined treatment with the antioxidant vitamins A (50,000 IU/day), **vitamin C** (1,000 mg/day), vitamin E (400 mg/day), and .beta.-carotene (25 mg/day) were compared for 28 days in 63 (intervention group) and 62 (placebo group) patients with suspected acute myocardial infarction. After treatment with antioxidants, the mean infarct size (creatine kinase and creatine kinase-MB gram equiv.) was significantly less in the antioxidant group than in the placebo group. Serum glutamic-oxaloacetic transaminase decreased by 45.6 IU/dL in the antioxidant group vs. 25.8 IU/dL in the placebo group ($p < 0.02$). Cardiac enzyme lactate dehydrogenase increased slightly (88.6 IU/dL) in the antioxidant group compared with that in the placebo group (166.5 IU/dL) ($p < 0.01$). QRS score in the ECG was significantly less in the antioxidant than in the placebo group. The following levels increased in the antioxidant group vs. the placebo group, resp.: plasma levels of vitamin E increased by 8.8 and 2.2 .mu.mol/L ($p < 0.01$), **vitamin C** increased by 12.6 and 4.2 .mu.mol/L ($p < 0.01$), .beta.-carotene increased by 0.28 and 0.06 .mu.mol/L ($p < 0.01$), and vitamin A increased by 0.36 and 0.12 .mu.mol/L ($p < 0.01$). Serum lipid peroxides decreased by 1.22

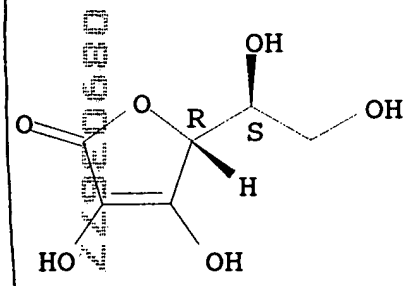
pmol/mL in antioxidant vs. 0.22 pmol/mL in the placebo group ($p < 0.01$). **Angina** pectoris, total arrhythmias, and poor left ventricular function occurred less often in the antioxidant group. Cardiac end points were significantly less in the antioxidant group (20.6% vs 30.6%, resp.). These results suggest that combined treatment with antioxidant **vitamins** A, E, **C**, and .beta.-carotene in patients with recent acute myocardial infarction may be protective against cardiac necrosis and oxidative stress, and could be beneficial in preventing complications and cardiac event rate in such patients.

IT **50-81-7**, **Vitamin c**, biological studies
(usefulness of antioxidant vitamins in suspected acute myocardial infarction)

RN 50-81-7 HCA

CN L-Ascorbic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 18-2 (Animal Nutrition)

IT Heart, disease
(**angina** pectoris, usefulness of antioxidant vitamins in suspected acute myocardial infarction)

IT **50-81-7**, **Vitamin c**, biological studies
1406-18-4, Vitamin e 7235-40-7, .beta.-Carotene 9001-60-9, Lactate dehydrogenase 11103-57-4, Vitamin a
(usefulness of antioxidant vitamins in suspected acute myocardial infarction)

L55 ANSWER 9 OF 22 HCA COPYRIGHT 1998 ACS

121:277888 Blood antioxidants and indices of lipid peroxidation in subjects with **angina** pectoris. Duthie, Garry G.; Beattie, James A. G.; Chb, Mb; Arthur, John R.; Franklin, Michael; Morrice, Philip C.; James, W. Philip T. (Scottish Agricultural Statistical Service, Rowett Research Institute, Bucksburn/Aberdeen, UK). Nutrition (Syracuse, N. Y.), 10(4), 313-16 (English) 1994. CODEN: NUTRER. ISSN: 0899-9007.

AB We tested the antioxidant hypothesis of coronary heart disease (CHD) by comparing blood antioxidants, indexes of lipid peroxidn. and classic (CHD) risk factors of 25 subjects with stable **angina** pectoris with 200 matched controls. **Angina** subjects had significantly increased plasma concns. of total cholesterol, low d.

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Volume (Issue):

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Year of Publication:

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Remarks: CAS - 127348-002
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=> d l53 1-2 cbib abs hitstr hitind

L53 ANSWER 1 OF 2 HCA COPYRIGHT 1998 ACS
126:338275 Nisoldipine coat-core: a review of its pharmacodynamic and pharmacokinetic properties and clinical efficacy in the management of ischemic heart disease. Langtry, Heather D.; Spencer, Caroline M. (Adis International Limited, Auckland, N. Z.). Drugs, 53(5), 867-884 (English) 1997. CODEN: DRUGAY. ISSN: 0012-6667. Publisher: Adis.

AB A review with 48 refs. Nisoldipine coat-core is an extended-release once-daily formulation of a dihydropyridine calcium antagonist effective in the treatment of chronic stable **angina** pectoris. With immediate-release formulations of nisoldipine, plasma drug concns. that produce therapeutic effects result rapidly, but are not sustained and do not maintain the effects throughout a 12-h dosage interval. In contrast, with nisoldipine coat-core, a gradual increase in plasma nisoldipine concns. occurs over 12 h and therapeutic concns. are then maintained for the duration of a 24-h dosage interval. In dosages of 10 to 60mg once daily, nisoldipine coat-core controls symptoms of **angina** and improves exercise-induced signs of ischemia in patients with stable **angina**. Compared with placebo, daily nisoldipine coat-core doses of.gtoreq.20mg provide statistically significant increases in total exercise time and time to produce **angina** and a trend towards an increase in the time to produce 1mm ST segment depression, in exercise tests conducted .apprxeq.23 h postdose. When administered in 20 and 40mg daily doses, nisoldipine coat-core produces improvements in exercise test parameters that are similar to those seen with amlodipine 5 or 10 mg/day or regular-release or sustained-release (SR) diltiazem 240 mg/day. The frequency of daily **angina** attacks and consumption of short-acting nitrates are also reduced by nisoldipine to a similar extent to that obsd. with these other agents. After longer term (1 yr) administration of 10 to 60mg daily, improvements in exercise test parameters are maintained, with equiv. anti-ischemic efficacy seen in patients

receiving nisoldipine coat-core alone or with background nitrate or .beta.-blocker therapy. Adverse events assocd. with nisoldipine coat-core are typical of the dihydropyridine class of calcium antagonists, with peripheral edema and headache being most common. Nisoldipine coat-core appears to be assocd. with fewer deaths than placebo, notably in the DEFIANT-II (Doppler Flow and Echocardiog. in Functional Cardiac Insufficiency: Assessment of Nisoldipine Therapy II) study, where only 1 death occurred with nisoldipine compared with 7 in the placebo group. Nisoldipine should not be taken during phenytoin therapy. In addn., **grapefruit juice** should be avoided during nisoldipine therapy and nisoldipine should not be taken concurrently with high-fat meals. Thus, the coat-core formulation of nisoldipine appears to have overcome the limitations of the shorter duration of action of immediate-release nisoldipine. Nisoldipine coat-core is well tolerated and once-daily administration produces a long duration of effective anti-ischemic relief in patients with chronic stable **angina** pectoris.

CC 1-0 (Pharmacology)

L53 ANSWER 2 OF 2 HCA COPYRIGHT 1998 ACS

74:115882 Citric acid pharmaceutical compositions. Renie, Jeanne Fr. M. FR 6334 681104, 4 pp. (French). CODEN: FMXXAJ. APPLICATION: FR 661213.

AB The use of citric acid (I) as a purgative, as a fluidizing agent for blood, or as a urine pH adjuster may give rise to toxic effects at the doses normally required. By using a combination of I with its alkali metal salts such side-effects are avoided. A formulation presented in a sachet contained 1.3 g I, 2 g mono-Na citrate, 2 g mono-K citrate, 1 mg tartrazine yellow, 40 mg **lemon essence**, 40 mg **orange essence**, 9 mg mandarin essence, and sucrose to 16 g. The compn. was useful in treatment of pain caused by **angina** and rheumatism.

IC A61K

CC 63 (Pharmaceuticals)

ST citrate compns **angina**; rheumatism citrate compns

=> d l55 1-22 ti

L55 ANSWER 1 OF 22 HCA COPYRIGHT 1998 ACS
TI Compositions and methods for inhibiting thrombogenesis

L55 ANSWER 2 OF 22 HCA COPYRIGHT 1998 ACS
TI Use of hydroxyguanidines for treatment or prevention of an ischemic disease

L55 ANSWER 3 OF 22 HCA COPYRIGHT 1998 ACS
TI Compositions and methods for inhibiting thrombogenesis

L55 ANSWER 4 OF 22 HCA COPYRIGHT 1998 ACS
TI Responses to acute myocardial stress and prior drug therapy on plasma levels of antioxidants and oxidants and the proposed role of

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DISEASE; HEART DISEASE; CLASS
50-81-7 (ASCORBIC ACID)
50-99-7 (GLUCOSE)
59-02-9 (ALPHA-TOCOPHEROL)
7235-40-7 (BETA-CAROTENE)
CC General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Biochemical Studies-Vitamins 10063
Biochemical Studies-Lipids 10066
Nutrition-Fat-Soluble Vitamins *13208
Cardiovascular System-Heart Pathology *14506
Cardiovascular System-Blood Vessel Pathology *14508
Blood, Blood-Forming Organs and Body Fluids-Blood and Lymph Studies *15002
BC Hominidae 86215

L32 ANSWER 9 OF 21 BIOSIS COPYRIGHT 1998 BIOSIS
AN 91:142181 BIOSIS
DN BA91:78721
TI RISK OF **ANGINA** PECTORIS AND PLASMA CONCENTRATIONS OF **VITAMIN** A **VITAMIN C** AND **VITAMIN** E AND CAROTENE.
AU RIEMERSMA R A; WOOD D A; MACINTYRE C C A; ELTON R A; GEY K F; OLIVER M F
CS CARDIOVASCULAR RES. UNIT, UNIVERSITY EDINBURGH, GEORGE SQUARE, EDINBURGH EH8 9XF, ENGL.
SO LANCET (N AM ED) 337 (8732). 1991. 1-5. CODEN: LANAAI
LA English
AB The relation between risk of **angina** pectoris and plasma concentrations of **vitamins** A, **C**, and E and carotene was examined in a population case-control study of 110 cases of **angina**, identified by the **Chest Pain** Questionnaire, and 394 controls selected from a sample of 6000 men aged 35-54. Plasma concentrations of **vitamins C** and E and carotene were significantly inversely related to the risk of **angina**. There was no significant relation with vitamin A. Smoking was a confounding factor. The inverse relation between **angina** and low plasma carotene disappeared and that with plasma **vitamin C** was substantially reduced after adjustment for smoking. Vitamin E remained independently and inversely related to the risk of **angina** after adjustment for age, smoking habit, blood pressure, lipids, and relative weight. The adjusted odds ratio for **angina** between the lowest and highest quantiles of vitamin E concentrations was 2.68 (95% confidence interval 1.07-6.70; p = 0.02). These findings suggest that some populations with a high incidence of coronary heart disease may benefit from eating diets rich in natural antioxidants, particularly vitamin E.
ST HUMAN LIPID AGE SMOKING CORONARY HEART DISEASE NATURAL ANTIOXIDANT-RICH DIET EPIDEMIOLOGY
RN 50-81-7 (VITAMIN C)

1406-18-4 (VITAMIN E)
68-26-8Q, 11103-57-4Q (VITAMIN A)
CC Behavioral Biology-Human Behavior *07004
Biochemical Studies-Vitamins 10063
Biochemical Studies-Lipids 10066
Nutrition-Fat-Soluble Vitamins *13208
Nutrition-Water-Soluble Vitamins *13210
Nutrition-General Dietary Studies 13214
Nutrition-Prophylactic and Therapeutic Diets *13218
Nutrition-Lipids 13222
Cardiovascular System-General; Methods 14501
Cardiovascular System-Heart Pathology *14506
Cardiovascular System-Blood Vessel Pathology *14508
Psychiatry-Addiction-Alcohol, Drugs, Smoking, etc. *21004
Toxicology-General; Methods and Experimental *22501
Gerontology *24500
Public Health: Epidemiology-Organic Diseases and Neoplasms *37054
BC Hominidae 86215

L32 ANSWER 11 OF 21 BIOSIS COPYRIGHT 1998 BIOSIS
AN 90:250224 BIOSIS
DN BR38:116812
TI LOW PLASMA **VITAMINS** E AND **C** INCREASED RISK OF **ANGINA** IN SCOTTISH MEN.
AU RIEMERSMA R A; WOOD D A; MACINTYRE C C A; ELTON R; GEY K F; OLIVER M F
CS CARDIOVASC. RES. UNIT, UNIV. EDINBURGH, EDINBURGH EH8 9XF, SCOTL.
SO DIPLOCK, A. T., ET AL. (ED.). ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, VOL. 570. VITAMIN E: BIOCHEMISTRY AND HEALTH IMPLICATIONS; CONFERENCE, NEW YORK, NEW YORK, USA, OCTOBER 31-NOVEMBER 2, 1988. XIII+555P. NEW YORK ACADEMY OF SCIENCES: NEW YORK, NEW YORK, USA. ILLUS. 0 (0). 1989 (1990). 291-295. CODEN: ANYAA9 ISBN: 0-89766-536-8(PAPER); 0-89766-535-X(CLOTH) ISSN: 0077-8923
DT Conference
LA English
ST HUMAN RISK ASSESSMENT SERUM CHOLESTEROL BLOOD PRESSURE SMOKING LOW FATTY ACID LEVELS PLASMA PHOSPHOLIPIDS ANTIOXIDANT
RN 57-88-5 (CHOLESTEROL)
CC General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Behavioral Biology-Human Behavior 07004
Biochemical Studies-General 10060
Biochemical Studies-Lipids 10066
Biochemical Studies-Sterols and Steroids 10067
Metabolism-Energy and Respiratory Metabolism *13003
Metabolism-Lipids *13006
Metabolism-Sterols and Steroids *13008
Metabolism-Fat-Soluble Vitamins *13016
Metabolism-Water-Soluble Vitamins *13018
Nutrition-Malnutrition; Obesity *13203
Nutrition-Fat-Soluble Vitamins *13208

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Remarks: LoC/DLC

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Medicinal compsn. for the treatment of **stenocardia** attacks contains (in wt.%): nonachazin(I)1.59-14.57; 96% ethanol 4.04-32.3; **ascorbic acid** 0.2-0.21; sodium metabisulphite 0.09-0.1; sodium chloride 0.24-0.26 and distilled water 65.54-80.86. The compsn. is quick-acting and reduces the severity and the duration of cardiac attack.

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L27 ANSWER 1 OF 1 BIOSIS COPYRIGHT 1998 BIOSIS
AN 80:130874 BIOSIS
DN BA69:5870
TI CONTINGENCY MANAGEMENT OF ADHERENCE TO A COMPLEX MEDICAL REGIMEN IN AN ELDERLY HEART PATIENT.
AU DAPCICH-MIURA E; HOVELL M F
CS LAB. STUD. BEHAV. MED., STANFORD UNIV. SCH. MED., SUITE 234, 730 WELCH RD., PALO ALTO, CALIF. 94304, USA.
SO BEHAV THER 10 (2). 1979. 193-201. CODEN: BHVTAK ISSN: 0005-7894
LA English
AB Whether token reinforcement could improve an elderly heart patient's adherence to his complex medical regimen was investigated. Using a multiple-baseline and reversal single-case experimental design, it was demonstrated that the reinforcement contingency was responsible for increasing his walking to more than twice/day, consumption of **orange juice** to an average of almost 3 glasses/day and consumption of 3 separate pills 3 times/day. A cessation of **angina** and an improvement in family relationships also occurred.
ST **ANGINA** FAMILY RELATIONSHIP TOKEN ECONOMY
CC Social Biology; Human Ecology 05500
Behavioral Biology-Human Behavior *07004
Behavioral Biology-Conditioning 07005
Physiology, General and Miscellaenous-Exercise and Physical Therapy 12010
Movement 12100
Pathology, General and Miscellaneous-Therapy 12512
Nutrition-General Studies, Nutritional Status and Methods 13202
Food Technology-Fruits, Nuts and Vegetables 13504
Cardiovascular System-Heart Pathology *14506

Please amend claim 1 as follows:

1. (amended) A method of preventing the reoccurrence of chest pain associated with the heart, which method comprises:

(a) noticing a pain in the chest; and then shortly thereafter

(b) taking an effective amount of lime juice into the body to alleviate the chest pain.

G2

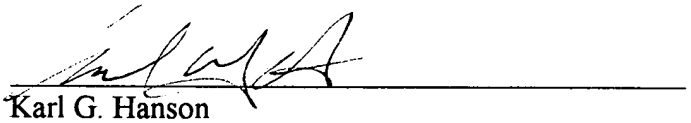
112 What is effective?

REMARKS

Claims 14-17 have been added to the application, and claim 1 has been amended to clarify the invention.

Dated this 12th day of January, 1998.

Respectfully submitted,



Karl G. Hanson
Attorney for Applicant
Registration No. 32,900

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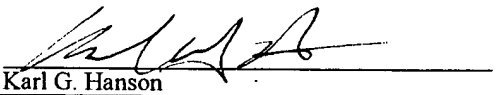

Karl G. Hanson

Dated: 1/12/98

What is claimed is:

1. A method of preventing the reoccurrence of chest pain associated with the heart, which method comprises:

(a) noticing a pain in the chest; and then shortly thereafter

(b) taking lime juice into the body to alleviate the chest pain.

2. The method of claim 1, wherein the chest pain is angina pectoris.

3. The method of claim 1, wherein the lime juice enters the body by consuming it orally.

4. The method of claim 2, wherein the lime juice is consumed in concentrated form by taking at least one half teaspoon of frozen concentrated lime juice or limeade.

5. The method of claim 1, further comprising:

preventing the reoccurrence of chest pain by taking lime juice into the body daily.

6. The method of claim 5, wherein at least one cup of lime juice is consumed orally daily.

7. The method of claim 6, wherein 2 to 5 cups are consumed daily.

8. The method of claim 6, wherein 2 to 3 cups are consumed daily.

9. A method of treating angina pectoris, which method comprises:

(a) noticing the onset of an angina attack; and then shortly thereafter

(b) taking an effective amount of lime juice into the body.

10. The method of claim 9, wherein the lime juice is taken orally.

11. The method of claim 10, wherein the lime juice is essentially pure lime juice.

12. The method of claim 10, wherein the lime juice is frozen concentrate for limeade.

13. The method of claim 10, wherein the lime juice is limeade.